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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/509,247	09/28/2004	Shunichi Kuroda	12480-000068/US	4500

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EXAMINER	
PENG, BO	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 12/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/509,247	KURODA ET AL.	
	Examiner	Art Unit	
	Bo Peng	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9/22/06*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-7,17 and 18* is/are pending in the application.

4a) Of the above claim(s) *4,5,7,17 and 18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/28/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Office acknowledges the receipt of Applicant's preliminary amendment filed on September 22, 2006. Claims 1, 2 and 4-7 are amended. Claims 3 and 8-16 are cancelled. New Claims 17 and 18 are added.

Communications Regarding Restriction/Election

2. The Office acknowledges the receipt of Applicant's restriction election, filed on September 22, 2006. Applicant elected Group I, with traverse. In response, Applicant's traverse is not relevant since the traverse was made based on the new amendment filed on September 22, 2006.

3. The previous *Election/Restrictions* is moot in view of the amendment filed on September 22, 2006. A new Restriction requirement has been set forth (see Paragraphs 5-13) and election has been made during the telephone interviews with attorney Donald Daley on November 29 and December 1, 2006. Applicant has confirmed the election of Group I, Claims 1, 2 and 6, and further elects the species of interferons in Claim 6. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). This restriction is made FINAL.

4. Accordingly, Claims 1, 2, 4-7, 17 and 18 are pending. Claims 4, 5, 7, 17 and 18 are withdrawn as nonelected. Claims 1, 2 and 6 are examined in the instant Office action.

Election/Restrictions

5. Restriction is required under 35 U.S.C. 121 and 372.

6. This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1, 2 and 6, drawn to the specific technical feature of a pharmaceutical compound comprising a particle-forming protein of HBV surface antigen.

Group II, claim(s) 4 and 17, drawn to the specific technical feature of a method for producing a HBsAg VLP.

Group III, claim(s) 5, 7 and 18, drawn to the specific technical feature of a method of treating a disease using HBsAg VLP.

Species Election

7. This application contains claims directed to more than one species of the generic invention. These species do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features. Applicant is required under 35 U.S.C. § 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

8. If Group I above is elected, Applicant is required to elect the target-cell substance is interferons, interleukins OR hapatocyte factors.

9. Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

10. Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

11. Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

12. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

13. In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

14. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Specification

15. Reference is made throughout the specification to nucleotide sequences, but SEQ ID NOs are not properly cited (for example, paragraphs [0077], [0093] and [0109] etc.). Correction is required.

Information Disclosure Statement

16. The information disclosure statement submitted on September 28, 2004 is in compliance with the provisions of 37 CRF 1.97. Accordingly, the information disclosure statement has been considered by the examiner. An initialed and dated copy of Applicant's IDS form 1449 is attached to the instant Office action.

Claim Rejections - 35 USC § 112, first paragraph

17. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

18. Claims 1, 2 and 6 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

"[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" Genentech Inc. v. Novo Nordisk 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997); In re Wright 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); See also Amgen Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir. 1991); In re Fisher 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Further, in In re Wands 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court stated:

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman [230 USPQ 546, 547 (BdPatAppInt 1986)]. They include (1) the quantity of

> experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

19. Claims 1, 2 and 6 are directed to a pharmaceutical compound comprising a particle-forming protein recognizing a specific cell or tissues; and a disease-treating target-cell-substance fused to the particle-forming protein, wherein the protein forms a nanoparticle encapsulating the target-cell-substance (Claim 1), wherein the particle-forming protein comprises a hepatitis B virus surface-antigen protein (HBsAg) (Claim 2), wherein the target-cell substance is an interferon (Claim 6).

20. Since there are no structural limitations to the particle-forming protein and target-cell-substance in Claim 1, the scope of the claims encompasses any particle-forming proteins containing any substances that can target cells or treat a disease. The state of prior art teaches that it is unpredictable to assemble a foreign protein or substance into a viral particle because formation of a viral particle requires specific packaging/assembly signals and has restrictions to insert sequences and sizes. The structure of foreign substances can affect particle formation. For example, Ward et al (Vir. Genes, Vol. 23: p. 97-104, 2001) tried to package the hepatitis C virus (HCV) core protein into HBsAg particles. Ward et al found that only limited chimeric proteins were packaged into viral particles, due to poor expression and the size limit to the insert (see in

particular the abstract and Fig. 3). Therefore, it is unpredictable in the art to assemble un-characterized substances into any particle-forming proteins. The specification has provided little guideline what are the structural requirements for "a disease-treating target-cell-substance" to be fused or packaged into any particle-forming proteins.

21. Moreover, in order to meet the function limitation of "a disease-treating target-cell-substance" of the claim, the substance encapsulated in the nanoparticles should maintain its "a disease-treating" activity or function. Although the specification has shown how to construct HBsAg/IFN (examples D and E), it has not characterized HBsAg/IFN particles. For example, it is not clear from the specification how many IFN molecules are fused into the HBsAg particle. Is the IFN fused with HBsAg biologically active? Without such teaching from the specification, one would not know whether or not fused "disease-treating target-cell-substance" with HBsAg can be used as a pharmaceutical compound for treating a disease.

22. Since Claim 1 clearly covers a broad range of viral particles containing "a disease-treating target-cell-substance", and in view of the empirical and unpredictable nature of the invention and lack of guidance and working examples in the specification, one skilled in the art cannot practice the claimed invention without undue experimentation.

Claim Rejections - 35 USC § 102

23. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

24. Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Valenzuela (1985, Biotechnology Vol.3, pp 323-326, cited in the IDS).

25. Claims 1 and 2 are directed to a pharmaceutical compound comprising a particle-forming protein recognizing a specific cell or tissues; and a disease-treating target-cell-substance fused to the particle-forming protein, wherein the protein forms a nanoparticle encapsulating the target-cell-substance (Claim 1), wherein the particle-forming protein comprises a hepatitis B virus surface-antigen protein (HBsAg) (Claim 2).

26. Valenzuela teaches a hybrid particle that contains both HBsAg and herpes simplex virus (HSV) surface antigen gD (HBsAg/HSV_{gD}).

27. Since gD is capable of interacting with an extended array of cell surface molecules, as evidenced by Campadelli-Fiume (2000, whole document), and overexpression of gD in BJ cell has shown to interfere with virus fusion and result in degradation of HSV virus (Campadelli-Fiume, 1988), HSV gD meets the limitation of "a disease-treating target-cell-substance" of Claim 1. Thus, the HBsAg/HSVgD meets the limitation of Claims 1 and 2. The instant Claims 1 and 2 are anticipated by Valenzuela.

28. Claims 1 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Kingsman (US 5,008,373).

29. Claims 1 and 6 are directed to a pharmaceutical compound comprising a particle-forming

protein recognizing a specific cell or tissue; and a disease-treating target-cell-substance fused to the particle-forming protein, wherein the protein forms a nanoparticle encapsulating the target-cell-substance (Claim 1), wherein the target-cell substance is an interferon (Claim 6).

30. Kingsman teaches a fusion protein, called as Ty:IFN-VPL, which comprising yeast TYA amino acid sequence and IFN amino acid sequence. Kingston teaches that Ty:IFN self-assembles into particles containing a plurality of Ty:IFN (Figure 7, columns 9 and 10).

31. Since Kingsman's Ty:INF-VPL meets the limitations of Claims that a disease-treating target-cell-substance fused to a particle-forming protein, wherein the treating target-cell-substance is an interferon, the instant Claims 1 and 6 are anticipated by Kinsman.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

32. Claims 1 and 2 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 24, 25, 28 and 30-33 of co-pending application of 10/220,125, Claims 1-7 and 9 of co-pending application 10/529,749 and Claims 1 and 2 of co-pending application 10/509,248. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to same process using the same products.

33. Claims 1 and 2 of the instant application are directed to a pharmaceutical compound comprising a particle-forming protein recognizing a specific cell or tissue; and a disease-treating target-cell-substance fused to the particle-forming protein, wherein the protein forms a nanoparticle encapsulating the target-cell-substance (Claim 1), wherein the particle-forming protein comprises a hepatitis B virus surface-antigen protein (HBsAg) (Claim 2).

34. Claims 24, 25, 28 and 30-33 of co-pending application of 10/220,125 are drawn to a hollow nanoparticle, comprising a protein particle obtained by expressing a hepatitis B virus surface antigen protein, or mutant thereof, capable of forming a particle in a eukaryotic cell, and a biorecognition molecule which is introduced into the hepatitis B virus surface antigen protein, or mutant thereof, wherein the biorecognition molecule is selected from the group consisting of cell function-regulating molecules, cell or tissue-recognizing molecules, antibodies and sugar chains, and wherein the hollow nanoparticle is capable of recognizing cells, wherein the biorecognition molecule is selected from the group consisting of growth factors, cytokines, cell surface antigens, tissue specific antigens, receptors and antibodies, wherein the eukaryotic cell is yeast or recombinant yeast, wherein the eukaryotic cell is an insect cell.

35. Claims 28 and 30-33 are directed to a transporter of substances, comprising a hollow

nanoparticle obtained by expressing a hepatitis B virus surface antigen protein or mutant thereof, capable of forming a particle in a eukaryotic cell, and a biorecognition molecule which is introduced into the hepatitis B virus surface antigen protein or mutant thereof, wherein the biorecognition molecule is selected from the group consisting of cell function-regulating biorecognition molecule, itself selected from the group consisting of growth factors, cytokines, cell surface antigens, tissue specific antigens, receptors and antibodies, wherein the substance to be introduced into cells is a gene, wherein the substance to be introduced into cells is a protein, wherein the substance to be introduced into cells is a compound.

36. Claims 1-7 and 9 of co-pending application 10/529,749 are drawn to hollow nanoparticles that comprise particle-forming first proteins, containing a bio-recognizing molecule for recognizing a specific cell, wherein at least one of the first proteins interacts with a second protein forming a capsid structure, wherein the first protein comprises a hepatitis B virus surface-antigen protein, wherein the first protein comprises a hepatitis B virus surface-antigen protein whose hepatocyte recognition site is modified to another bio-recognizing molecule, wherein the first protein comprises a hepatitis B virus surface-antigen protein whose hepatocyte recognition site is modified to a beta-cellulin or a basic fibroblast growth factor, wherein thesecond protein comprises a hepatitis B virus core-antigen protein, wherein the hollow nanoparticles are formed by transferring a gene encoding the first protein and a gene encoding the second protein to a single eukaryotic cell by separate vectors, so that the respective genes are co-expressed in the eukaryotic cell, wherein the eukaryotic cell is a yeast cell. A drug that is made of the hollow nanoparticles, as set forth in Claim 1, wherein a target cell substance is encapsulated in the hollow nanoparticles.

37. Claims 1 and 2 of co-pending application 10/509,248 are directed to a drug, comprising a substance to be transferred into a cell for treatment of a disease encapsulated in a hollow nanoparticle containing a particle-forming protein, the nanoparticle displaying a molecule, such as a growth factor, which binds with a specific molecule on a cell surface, wherein the protein is a modified hepatitis B virus surface antigen protein.

38. Since the four sets of claims are all drawn to nanoparticles comprising HBsAg and a compound that recognizes/targets bio-systems or cells, they clearly are the same compounds. Therefore, the pharmaceutical compound of the instant Claims 1 and 2 are not patentably distinct from those of 10/220,125, 10/529,749, and 10/509,248.

Remarks

39. No claims are allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bo Peng, Ph.D. whose telephone number is 571-272-5542. The examiner can normally be reached on M-F, 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, Ph.D. can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Bo Peng, Ph.D.
12/7/06

Bruce Campell

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